Journal of Obstetrics, Gynecology and Cancer Research | ISSN: 2476-5848

A Case Report of Complete and Prolonged Response to Hormonal Therapy in Recurrent Metastatic Endometrial Cancer

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Article Info

10.30699/jogcr.3.4.30

Received: 2018-05-08;
Accepted: 2018-06-03;
Published Online: 16 Sep 2018;

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ABSTRACT

Background & Objective: Endometrial cancer is one of the most common gynecologic malignancies in developed countries. Survival rate in metastatic endometrial adenocarcinoma recurrence is reduced, and treatment in these patients is mostly palliative. One of the therapeutic options in the endometrial adenocarcinoma recurrence is hormone therapy. The expected response to the hormonal treatment is about 10-20%.

Case Report: This is a case report from 57-year-old woman suffering from stage IA - Grade 1 endometrial cancer, who had vaginal carcinoma recurrence with liver and pulmonary metastasis 5.5 years after the initial treatment. Due to positive hormone receptor and the pathological profile of the tumor, hormone therapy with tamoxifen and megestrol was started. The treatment evaluation revealed complete response within five months with clearance of lung and liver metastatic lesions. There is no evidence of disease and metastases in the patient's examination and imaging after 3 years of starting hormone therapy.

Conclusion: In the case of well-differentiated recurrent and metastatic endometrial cancer, good response to the hormone therapy by the least complications might be achieved.

Keywords: Endometrial neoplasms; Recurrence; Endocrine therapy

Introduction

Endometrial adenocarcinoma is the most common type of gynecologic malignancy in developed countries, and the second common type in developing countries. Regardless of the type of treatment, survival rate in metastatic endometrial cancer is reduced **(1)**. Chemotherapy and hormone therapy are therapeutic options in treating these patients. In hormone therapy, the expected response rate is 10-20%, and survival is estimated to be less than one year. Since comorbidity and poor performance in these patients are common, hormone therapy could be an appropriate alternative in the patients with well-differentiated tumors with long disease-free intervals **(2)**. This is a case report of an endometrial cancer patient with vaginal recurrence and metastasis to the lung and liver, with complete and long response to the hormone therapy.

Case Report

A 57-year-old woman was subjected to the curettage with post-menopausal bleeding in 2011, with pathologic report of endometrioid adenocarcinoma. Based on this pathology report, total abdominal hysterectomy and bilateral salpingo-oophorectomy (TAH, BSO) and complete staging surgery including pelvic and bilateral para-aortic lymphadenectomy was done. Intraoperative findings were right ovarian cyst, with a mass in the left kidney. According to the urological consultation, partial nephrectomy was done. Pathologic report was consistent with endometrial carcinoma, stage IA - Grade I and oncocytoma in the left kidney.

According to the usual planning for the oncology patients at Imam Hussein Medical Centre, the treatment was decided based on the NCCN's Guideline at a joint medical meeting. The patient was followed up without any adjuvant treatment. The patient follow-ups were conducted regularly until 2016, when vaginal spotting was reported. In the physical examination, a solid mass on the right side of the vaginal cuff, in the size 3-4 cm existed. In the abdominal and pelvic MRI, a cystic mass with a fluid level of 30 mm by 18 mm in the right upper wall of the vaginal cuff was observed with adhesion to the rectum. The transvaginal ultrasound (TVS) showed two round masses with a total dimension of 25 × 13 mm in the right side of the vaginal cuff.

The patient underwent vaginal cuff biopsy from the mass. The pathologic report was endometrioid adenocarcinoma of Grade I and confirmed the

recurrence. In radiologic imaging, the chest CT scan, revealed multiple nodules in the left lung field with a maximum size of 2 cm. In the abdominal CT scan, a lesion of 6 mm size in the segment of 7 in liver was found suggesting metastasis. In PET SCAN, lesions with metabolic activity were reported in the field of both lungs and in the right lobe of the liver, segment 7, and in the vaginal cuff suggestive of the liver tumor tissue. The CA125 was normal with titer of 3.7. The biopsy of pulmonary lesions confirmed metastasis, metastatic well-differentiated adenocarcinoma. The IHC was negative for PR, and ER was strongly positive and p63 was reported as weakly positive.

The patient was treated with hormone therapy including tamoxifen 20 mg twice daily plus 40 mg megestrol 4 times per day every 3 weeks as alternative. The follow up of the patient was done by examination of the size of the vaginal mass, checking the CA125 and measuring the size of the lung and liver metastasis. Hormone therapy was well tolerated and continued.

In follow-up studies for the patient, 5 months after the start of treatment, pulmonary lesions in the chest CT scans were completely eliminated, and liver mass was absent in MRI. The size of the vaginal mass decreased from 4 centimeters to 1 centimeter in clinical examinations. In the TVS study, the size of the vaginal mass decreased from 3 cm to 1 cm. So far, there has been no change in vaginal mass size, it can be speculated that the remaining tissue is probably fibrosis. The CA125 level in the pursuit is still normal. The patient is still under 3 years follow up, and hormone therapy continues, with stable disease and no evidence of recurrence.

Discussion

Uterine cancer is one of the most common gynecological cancers in the United States **(3)**. In 2012, about 52,776 uterine cancer cases were detected worldwide, with an estimated mortality rate of 1.7 to 2.4 per 100,000. Among reported pathologies, endometrial adenocarcinoma is the most common type of the disease **(4).** Overally, endometrial cancer can be considered as a high-cured disease **(5)**. Five year survival for the localized disease is about 96%, and 67% for the regional disease, and about 17% for the patients with metastatic disease **(3)**.

Most cases of the recurrence occur within the first 3 years of the diagnosis **(1)**. On the present case, recurrence occurred 5.5 years after treatment of the primary disease. The recurrence symptoms are mostly non-specific, and in most women, symptoms such as vaginal, rectal bleeding or hematuria, loss of appetite, weight loss or bone and pelvic pain, cough and distant metastasis symptoms occur **(1)**. The present case symptom of recurrence was vaginal spotting.

Recurrence of the endometrial cancer is diagnosed using clinical examination, radiologic and laboratory findings. Any visible lesions in the examination should be biopsied and the relapse of the disease should be investigated **(6)**. Treatment for the endometrial cancer recurrence is not curative, regardless of histology. Two exceptions are the isolated vaginal cuff recurrence in a field that has not previously undergone radiotherapy and an isolated lung metastasis that can be surgically resected **(7)**.

Therapeutic options in these patients include surgery, radiotherapy, chemotherapy and hormone therapy. The choice of treatment in these patients is based on the history of primary treatment, the extent and localization of the disease, the size of the tumor, the state of the hormone receptor of the tumor and the patient's performance status **(8)**. As noted above, the treatment of these patients in most cases is palliative, and we expect low response and short survival rates in these patients **(9)**.

As mentioned, one of the treatment options in these patients is hormone therapy, which is used either as a primary treatment or after cytoreductive surgery or chemotherapy. In the patients with Grade I or II tumors, positive hormone receptor and in asymptomatic patients or with low symptoms, hormone therapy is acceptable **(1)**. Among other factors that have been identified with the appropriate response to hormone therapy, there is a long period between initial treatment and hormone therapy and low burden of the disease **(9)**.

The recurrence occurred in the present case 5.5 years after the initial treatment. This treatment was well tolerated and showed a low toxicity in comparison with chemotherapy. Several types of progestins have been identified in the treatment of recurrent metastatic endometrial cancers. These include hydroxyprogesterone caproate with 9-43% response, medroxyprogesterone acetate with 14- 53% response, and megestrol acetate with 11 -56% responding to the treatment. Based on the theory, estrogenic compound causes up-regulation of the progesterone receptors in the endometrial tumor, and can also be used to increase the progesterone effect in the patient with recurrent or metastatic endometrial cancer. The recommended estrogenic substance is tamoxifen **(10)**. It has been shown that the route of administration of progesterone substance did not affect the survival rate of these patients, and overall survival was similar in both injection and oral administration types **(9)**. By considering poor prognosis in the patients with metastasis, hormone therapy produces total response rate of 27% and progression-free survival of 2.7 months, and the mean overall survival of 14 months **(1)**. Various studies have been done to compare the treatment response of different

progestin substances in these patients. Two studies were conducted by the GOG group.

In a prospective study, patients with the advanced endometrial cancer were treated with tamoxifen 20 mg twice daily with alternate weekly concomitant Medroxy progesterone acetate 100 mg twice daily. The result showed 33% response to the treatment and an overall survival was 3 months **(10)**. In another study, patients were treated with megestrol 80 mg twice daily for three weeks followed by 20 mg tamoxifen twice daily for three weeks. In this study, the overall response to the treatment was 26% **(11)**.

Conclusion

In the present case, after three years of the onset of hormone therapy in the recurrence treatment of endometrial cancer with metastasis to the lung and liver, no evidence of recurrence or metastasis was observed. The treatment was well tolerated and there was no evidence of drug side effects. The characteristic feature of the patient was a long and complete response (at least 3 years to now) to the hormone therapy.

With proper selection of the patients with metastatic endometrial cancer with positive hormone receptor and low-grade histology, hormonal therapy can be considered as an effective treatment with low toxicity.

Acknowledgements

The authors would like to thank all those who helped them writing this paper.

Conflict of Interest

Authors declared no conflict of interests.

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How to Cite This Article:

Faghih N, Arab M. A Case Report of Complete and Prolonged Response to Hormonal Therapy in Recurrent Metastatic Endometrial Cancer. jogcr. 2018; 3 (4) :169-171

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